Stratton VA Medical Center
IRB Standard Operating Procedure: Human Research Protection Program (HRPP) Overview

MISSION

The mission of the Stratton VA Medical Center's Human Research Protection Program (HRPP) is to assure participants of research studies that their rights and welfare will be protected by the Institution through the oversight of the Institutional Review Board (IRB), the Research and Development (R&D) Committee and the Research Compliance Department.

OVERVIEW

The objective of the HRPP is to assist the Stratton VA Medical Center (VAMC) in meeting ethical principles and regulatory requirements for the protection of human subjects in research. The Institution is also assisted by the Office of Research and Development (ORD), The Program for Research Integrity Development and Education Program (PRIDE) and the Office of Research Oversight (ORO).

Under the HRPP, human subject research activities at the Stratton VAMC are guided by the ethical principles as described in the Belmont Report, (Respect for Persons, Beneficence and Justice) and as implemented by the Common Rule [56 Federal Register (FR) 28001, which is incorporated into Title 38 Code of Federal Regulations (CFR) part 16]. This commitment is also consistent with the principles described in the Nuremberg Code and the Declaration of Helsinki. It is an obligation and expectation that all Stratton VAMC staff with responsibilities in the HRPP will adhere to the ethical principles as described in the Belmont Report.

This HRPP is made up of a number of elements. This policy will discuss the relationships of the various elements to the HRPP. Full descriptions and procedures for a number of these elements are contained in other documents (VA and Federal regulations, polices and SOPs). These other documents are an important part of the HRPP and are referenced throughout this policy.

The Human Research Protection Program (HRPP) at the Stratton VAMC is coordinated with a line of authority from the Institutional Official to the various components of the HRPP.

All appropriate actions will be taken to ensure accountability in research for protection of human subjects, as required by the Federal Wide Assurance (FWA) with the Office for Human Research Protections (OHRP). The Stratton VAMC IRB is the IRB of Record for the Bath VAMC and the Albany Research Institute (VA non-profit).

- Stratton VAMC – FWA 00002073; IRB 00000950
- Bath VAMC – FWA 00002072
- Albany Research Institute – FWA 00001876

All investigators and research staff must comply with policies and decisions of the Institutional Review Board (IRB) and organizational policies, standard operating procedures and regulations for patient rights, the protection of human subjects, and the ethical conduct of research.

Establishing an appropriate research environment requires an ongoing effort to educate researchers, their staff, research administrators, IRB members, VA R&D Committee members, institutional officials, and study participants about research ethics and other HRPP issues. This HRPP policy is part of the effort to ensure an ethical research environment including accountability, regulatory compliance, ethics training, transparency, and open communication.

The ethical conduct of research is a shared responsibility. It requires cooperation, collaboration, and trust among the institution, investigators and their staff, the subjects who enroll in the research, and the IRB and R&D members and staff. The HRPP involves a number of positions and committees with responsibilities for human research protection including (but not limited to):

- The Medical Center Director
- Chief of Staff
- Associate Chief of Staff for Research & Development (ACOS/R&D)
- The R&D Committee
- The IRB Committee
- Other Committees Or Subcommittees Addressing Human Subjects Protection
  [e.g., Subcommittee on Research Safety and Biosafety (SRS&B), Radiation Safety Committee]
- Administrative Officer for Research (AO/R)
- Research Committee Coordinators
- HRPP Coordinator
- Research Service Administrative Staff
- Research Compliance Officer
- Investigators
- Research staff
- Research Pharmacy Staff

- Health And Safety Staff (e.g., Biosafety Officer, Radiation Safety Officer)
- Privacy Officer
- Patient Advocate(s)
- Office of Performance Measurement
- Patient Safety Officer
- Risk Manager
- Ethics Advisory Committee

The VA Medical Center Institutional Review Board's (IRB) Standard Operating Procedure (SOP) is a reference for investigators and IRB members. This manual was developed to serve two purposes:

1. to describe the functions and procedures followed by the Institutional Review Board (IRB) of the Research and Development (R&D) Committee at the Stratton VA Medical Center, Albany, New York, and

2. to outline for investigators the procedures and requirements for submitting human research proposals for review by the IRB, and for the subsequent conduct of that research.

The Institutional Review Board (IRB) enforces the federal policies and procedures as dictated by the Department of Veterans Affairs (VA Headquarters and the local facility) and also by the Office for Human Research Protection (OHRP) and the Food and Drug Administration (FDA), under the auspices of the US Public Health Service. The DVA is one of 16 departments and agencies that have adopted the Federal Policy for the Protection of Human Subjects (also known as The Common Rule).

This Standard Operating Procedure (SOP) will be reviewed at least annually to incorporate any changes necessary in response to VA and/or federal regulations regarding protection of human subjects. The IRB, the Research and Development Committee, and others, as needed, will participate in the review.

The IRB is part of the systematic and comprehensive "Human Research Protection Program" (HRPP) at the Stratton VA Medical Center, with dedicated resources to ensure the rights, safety, and well being of human research subjects participating in research activities.

The HRPP is a comprehensive system that ensures the protection of human subjects participating in research. The program consists of a variety of individuals and committees such as: the Medical Center Director, Associate Chief of Staff (ACOS) for Research and Development (R&D), the Administrative Officer (AO) for R&D, Research Compliance Officer, the R&D Committee, the IRB, other committees addressing human subject protection (e.g., Biosafety, Radiation

Safety), investigators, IRB staff, research staff, health and safety staff (e.g. Safety Officer, Radiation Safety Officer) and research pharmacy staff.

The HRPP program also includes a research compliance plan (informed consent/HIPAA reviews, participant surveys, and study audits) and an assessment of resources plan. The Research and Development (R&D) Committee will annually review the budgeting process and the organizational structure for human subjects research (HRPP Resource Plan) to ensure adequate resources are available to promptly carry out its functions. The annual review will encompass an evaluation of the volume of research, FTE, computer resources, meeting area, filing space, reproduction equipment, databases, supplies, office space, capital equipment, training and education, and any other items as needed. The annual evaluation is submitted to the Research & Development Committee for review and approval, and reviewed by the Medical Center Director in the R&D minutes.

All research performed at the Stratton VA Medical Center will have the approval of the Research & Development Committee irrespective of the status of approval or activity of the research at other sites (multi-site studies). For research conducted at multiple sites, there must be a site investigator in Albany who will report the adverse events for the entire study to the Albany IRB. When human research is a component or the sole purpose of the study, the review and approval process by the IRB will take place according to the policies and procedures of the Stratton VA Medical Center.

The HRPP program will seek and maintain AAHRPP accreditation. Most human research protection program documents and policies are on the research website.

MEMORANDUMS OF UNDERSTANDING (MOU'S)

Stratton VAMC and Bath VAMC MOU

Bath VAMC is granted the full use of the Stratton VAMC's Research Service. This MOU enables Bath to participate in research projects without creating a separate and independent research service at Bath.

1. The Stratton VAMC and the Bath VAMC shall file its own individual Federal Wide Assurance (FWA) through the Office of Research Oversight to OHRP.
2. The Stratton IRB and R&D committees shall include a voting representative from Bath.
3. The Stratton IRB shall register with OHRP and serve as the "IRB of Record" for both Albany and Bath.

ESSENTIAL COMPONENTS OF THE HRPP (Including, but not limited to)

Federal Wide Assurance (FWA) – an assurance of protection for human subjects that:

- is granted by the Department of Health and Human Services (DHHS).
- Ethical Principles – The Belmont Report, 45 CFR 46 and all of its subparts (A, B, C, D) and the Common Rule.
- VHA Handbook 1200.5
- Comprehensive review of research protocols by the IRB and R&D committees and if necessary, the SRS&B and Radiation Safety Committees. No research involving human subjects may commence without all appropriate research sub-committee approvals and final, written approval by the R&D Committee. An IRB-approved research activity may be disapproved by the R&D Committee, the Medical Center Director, or ORD. The organization does not allow officials to approve research that has not been approved by the IRB.
- Informed Consent Process
- Ongoing (Risk Appropriate) Safety Monitoring by the IRB and R&D Committees, and other applicable committees/offices
- Auditing/Quality Improvement
- Education And Training Of Investigators And Research Staff
- Conflict Of Interest Management
- Procedure For Receiving And Responding To Complaints And Allegations Of Non-Compliance
- Credentialing
- Standard Operating Procedures And Policies for the IRB and R&D Committees
- The HRPP program also includes a research compliance plan (informed consent/HIPAA reviews, participant surveys, and study audits) and an assessment of resources plan. The Research and Development (R&D) Committee will annually review the budgeting process and the organizational structure for human subjects research (HRPP Resource Plan) to ensure adequate resources are available to promptly carry out its functions. The annual review will encompass an evaluation of the volume of research, FTE, computer resources, meeting area, filing space, reproduction equipment, databases, supplies, office space, capital equipment, training and education, and any other items as needed. The annual evaluation is submitted to the Research & Development Committee for review and approval, and reviewed by the Medical Center Director in the R&D minutes.
- The HRPP program will seek and maintain AAHRPP accreditation. Most human research protection program documents and policies are on the research website.

ACTIVITIES SUBJECT TO THE HRPP

Activities are considered to be human subject research and therefore subject to the HRPP if they meet the definition of research and human subject as defined according to the Department of Health and Human Services (DHHS) and the Department of Veterans Affairs (DVA) definition OR if they meet the definition of research (clinical investigation) and human subject as defined according to the Food and Drug Administration (FDA) definition.

DHHS and DVA

"Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Research subject to regulation, and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or non-research in nature [for example, Wage and Hour requirements administered by the Department of Labor,." Section 16.102(e)].

"Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) Data through intervention or interaction with the individual, or (2) Identifiable private information. Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject."

"Private Information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects" (Section 102(f).

FDA

All research involving FDA regulated drugs, devices and biologics (regardless of funding source) are subject to the regulations found at Title 21CFR 50 and 56 and CFR 54, 312, 314, 600, 812, and 814 as applicable.

Per FDA Title 21 CFR 50 and 56: Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Dreg Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory. An activity is FDA regulated research when:

1. It involves the use of a drug (approved or unapproved), except for the use of an approved drug in the practice of medicine.
2. It involves the testing of the safety or efficacay of a medical device.
3. The date will be reported to or held for inspection by FDA.

Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. Under 21 CFR 812 this also includes an individual on whose specimen an investigational device is used.

Test article means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354F of the PHS ACT (21CRF50.3(j); 21 CFR 56 102(l)

CONDITIONS UNDER WHICH HUMAN RESEARCH BECOMES SUBJECT TO THE HRPP

Human research becomes subject to our HRPP when research (exempt and non-exempt) involving human subjects is conducted completely or partially in VA facilities, conducted in approved off-site locations/facilities and/or conducted by VA researchers while on VA official duty time. This also includes recruitment of VA patients to research protocols conducted elsewhere by VA investigators while on duty at VA facilities or approved off-site locations. The research may be VA funded, funded from extra-VA sources, or conducted without direct funding. The research uses this institution's non-public information to identify or contact human research subjects or prospective subjects (enrolling VA patients).

Agents of the Organization – all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility. The Stratton VAMC is considered "engaged" in human subjects research under our FWA and subject to our HRPP when the institution's involvement includes the following:

1. Stratton VAMC employees or agents intervene with living individuals by performing invasive or noninvasive procedures for research purposes (e.g., drawing blood; collecting other biological samples; dispensing drugs; administering other treatments; employing medical technologies; utilizing physical sensors; utilizing other measurement procedures).

2. Stratton VAMC employees or agents intervene with living individuals by manipulating the environment for research purposes (e.g., controlling environmental light, sound, or temperature; presenting sensory stimuli; orchestrating environmental events or social interactions; making voice, digital, or image recordings).

3. Stratton VAMC employees or agents interact with living individuals for research purposes (e.g., engaging in protocol-dictated communication or interpersonal contact; conducting research interviews; obtaining informed consent).

4. Stratton VAMC employees or agents release individually identifiable private information, or permit investigators to obtain individually identifiable private information, without subjects' explicit written permission (e.g., releasing patient names to investigators for solicitation as research subjects; permitting investigators to record private information from medical records in individually identifiable form).

5. Stratton VAMC employees or agents obtain, receive, or possess private information that is individually identifiable (either directly or indirectly through coding systems) for research purposes (e.g., obtaining private information from medical records in an individually identifiable form).

6. Stratton VAMC employees or agents obtain, receive, or possess private information that is individually identifiable (either directly or indirectly through coding systems) for the purpose of maintaining "statistical centers" for multi-site collaborative research.

7. Stratton VAMC receives a direct HHS award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator (e.g., a small business receives a HHS award to design a medical device at its own facility and contract with a medical clinic to test the device with human subjects; a foundation receives a HHS award on behalf of an affiliated institution that will actually conduct the human subjects research).

TYPES OF RESEARCH TYPICALLY COVERED BY THE HRPP

Research conducted at the Stratton VAMC is generally designed to advance health care for our veteran population and the nation. The human research protection program typically covers the following types of research: Biomedical Laboratory, Clinical Science (including VA Cooperative Studies), Health Services, Rehabilitation, Behavioral, Psychological, and industry-sponsored Clinical Trials.

Categories of Participants Typically Covered by the HRPP:

- Research subjects are generally veterans receiving health care from the VA, care givers, healthy volunteers and those with conditions that affect the veteran population. Typical research subjects are adults with independent decision-making capacity.

- Non-veterans may be entered into VA-approved research studies only when there are insufficient veterans available to complete the study in accordance with 38 CFR 17.45 and 38 CFR 17.92. All regulations pertaining to the participation of veterans as research subjects including requirements for indemnification in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research.

- Stratton VAMC research program does not participate in research with children and/or prisoners. The IRB will be particularly cognizant of the special problems of research involving vulnerable populations such as: disabled persons or persons with impaired decision-making capacity, and economically or educationally disadvantaged.

AUTHORITY FOR THE HRPP

The Stratton VAMC maintains a Federal Wide Assurance (FWA) and has registered its IRB with the Department of Health and Human Services (DHHS)

Office of Human Research Protection (OHRP) through the VA Office of Research Oversight (ORO).

The signatory official for the FWA is the Director of the Stratton VAMC. The FWA documents the Stratton VAMC's commitment to human subjects protection regarding: ethical principles, review of research, informed consent, training, local procedures, resources and staffing. Assurance is also given that human research for which the IRB provides review and oversight will comply with Federal Policy (the "Common Rule" Title 45 Code of Federal Regulations (CFR) Part 46 and Title 38 CFR 16).

In keeping with the FWA, the Stratton VAMC has done and pledges to do the following:

1. Develop and maintain policies and procedures for the human subjects protection program.
2. Designate the Stratton VAMC Institutional Review Board (IRB) to review all research covered by the Assurance.
3. Provide sufficient resources, space and staff to support the IRB's review and record keeping duties.
4. Provide training and education for the IRB and Investigators.

In addition to the FWA, authority for the HRPP comes from the following regulations:

5. VHA Handbook 1200.05 Requirements for the Protection of Human Subjects in Research
6. VHA Handbook 1200.01 Research & Development Committee
7. VHA Pharmacy Manual, M-2, Part VII, Chapter 6 and Chapter 5.10
8. Statutory provision for protection of VA patient rights (38 USC Sections 501, 7331 and 7334)
9. VA regulations pertaining to protection of patient rights (38 CFR 17.33a and 17.34)
10. VA regulation pertaining to rights and welfare of human subjects participating research (38 CFR 16 - Federal Policy for the Protection of Human Subjects – The Common Rule)
11. VA regulations pertaining to research related injuries (38 CFR 17.85)
12. VA regulations pertaining to hospital care for research purposes and outpatient care for research purposes (38 CFR 17.45, 17.92)

13. Statutes and regulations pertaining to the release of patient information (5 USC § 522a; 38 USC §§ 5701a, 7332; 45 CFR Parts 160-164)
14. Department of Health and Human Services (DHHS) regulations pertaining to rights and welfare of human subjects participating in research supported by DHHS (45 CFR 46)
15. Food and Drug Administration (FDA) regulations pertaining to rights and welfare of human subjects participating in research involving investigational drugs and devices (21 CFR parts 11, 50, 56, 312, 812, and 814)
16. Nuclear Regulatory Commission (NRC) regulations pertaining to medical use of byproduct material and protection of human subjects: 10 CFR Parts 20 (Standards for Protection Against Radiation) and 35 (Medical Use of Byproduct Material).
17. VA confidentiality of medical quality assurance records statue: 38 U.S.C. 5705.

New York State Statutory Structure Regarding Clinical Trials

With regard to clinical trials, New York State has adopted standards that primarily mirror federal requirement. Additionally, all such trials may be conducted only by appropriately licensed researchers affiliated with the Stratton VA Medical Center, which has a human research review committee, the Institutional Review Board (IRB).

1. Protocols should be designed to comply with federal regulations.
2. VHA Handbook 1200.5 states that children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
   Age of majority is 18 years of age. NY Gen. Oblig. Law § 1-202 (2004). Health care consent may be provided by persons 18 years of age or older.
3. New York mandates that voluntary informed consent be provided in writing by every person who will participate in a research study. NY Public Health Law § 2442 (2004). Federal guidelines allow for waiving the requirement that the subject sign a written consent. (Title 21, Part 56.109).
4. Each New York institution that conducts or approves clinical research must establish a human research review committee. The Stratton VA Medical Center has their own IRB. NY Public Health Law § 2444 (2004).
5. There are no special rules for cancer research specified within New York's statutes or regulations.

6. There are no specified New York statutes or regulations regarding reimbursement of clinical trial subjects.

7. HIV Testing Rules – No physician or other person may order an HIV test without first obtaining written informed consent, unless the testing is for research, the test preserves the patient's anonymity, and the patient's identity cannot be retrieved by the researcher. NY Public Health Law § 2781 (2004); 10 N.Y.C.R.R. 63.3 (2004). Participating in any human subjects research sponsored by VA, as well as any human subjects research conducted on VA premises, must meet the requirements of VHA Handbook 1200.5 and the SOP IRB-010.
8. An investigational drug may be used by scientific experts, provided that the drug is plainly labeled, "For investigational use only". NY Educ. Law 6817 (2004). The federal regulations require "Caution: New Drug-Limited by Federal Law to Investigational Use".

HUMAN RESEARCH

Ethical Mandate to Protect Human Subjects

The basic ethical principles guiding research involving human subjects are described in the following documents.

- **The Nuremberg Code.** The modern history of human subject protections begins with the discovery after World War II of numerous atrocities committed by Nazi doctors in war-related human research experiments. The Nuremberg Military Tribunal developed ten principles as a means of judging their "research" practices, known as *The Nuremberg Code*. The significance of the Code is that it addressed the necessity of requiring the voluntary consent of the human subject and that any individual "who initiates, directs, or engages in the experiment" must bear personal responsibility for ensuring the quality of consent.

- **The Declaration of Helsinki.** Similar principles to The Nuremberg Code have been articulated and expanded in later codes, such as the World Medical Association *Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects (1964, revised 1975, 1983, 1989, 1996, 2000, with a footnote added in 2002),* which call for prior approval and ongoing monitoring of research by independent ethical review committees.

- **The Belmont Report.** Revelations in the early 1970s about the 40-year United States Public Health Service Study of Untreated Syphilis in the Negro Male at Tuskegee and other ethically questionable research resulted in 1974 legislation calling for regulations to protect human

subjects and for a national commission to examine ethical issues related to human subject research (i.e., the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research).

- The Commission's final report, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, defines the ethical principles and guidelines for the protection of human subjects.

  Perhaps the most important contribution of *The Belmont Report* is its elucidation of three basic ethical principles:

  - Respect for persons (applied by obtaining informed consent,
  - consideration of privacy, confidentiality, and additional protections for vulnerable populations);
  - Beneficence (applied by weighing risks and benefits); and
  - Justice (applied by the equitable selection of subjects).

  The Belmont Report also provides important guidance regarding the boundaries and interface between biomedical research and the practice of medicine.

REGULATORY MANDATE TO PROTECT HUMAN SUBJECTS

Department of Veterans Affairs (VA) and other Federal regulations require specific protections for human subjects:

a. **Department of Health and Human Services (DHHS) Regulations at 45 CFR 46.** In May of 1974, the Department of Health, Education, and Welfare (later renamed DHHS) codified its basic human subject protection regulations at 45 CFR 46, Subpart A. Revised in 1981 and 1991, the DHHS regulations presently include additional protections for fetuses, pregnant women, and human in vitro fertilization (Subpart B), prisoners (Subpart C), and children (Subpart D). The DHHS regulations are enforced by the Office for Human Research Protections (OHRP).

b. **Department of Veterans Affairs (VA) Regulations at 38 CFR 16 and the Federal Policy (Common Rule) for the Protection of Human Subjects. In addition, 38 CFR 17.33 provides regulations for patient rights. 38 CFR 17.85 discusses treatment of research related injuries to human subjects. 38 CFR 17.45 is Medical Hospital Care for Research Purposes. 38 CFR 17.92 is Outpatient Care for Research Purposes.** In January of 1991, the VA joined 16 other Executive Branch Departments and Agencies in simultaneously adopting the Federal Policy (Common Rule) for the Protection of Human Subjects. Codified by the VA

at 38 CFR 16, the Common Rule is the same as that codified by DHHS as Subpart A of the DHHS regulations at 45 CFR 46, but does not include the additional DHHS Subparts.

c. **Food and Drug Administration (FDA) Regulations at 21 CFR 50 and 56.** When DHHS revised its regulations in 1981, the FDA codified almost identical informed consent regulations at 21 CFR 50 and IRB regulations at 21 CFR 56. Additional FDA regulations that are relevant to the protection of human subjects are:

(1) Investigational New Drug Applications (IND) (21 CFR 312)

(2) Radioactive Drugs (21 CFR 361)

(3) Biological Products (21 CFR 600)

(1) Investigational Device Exemptions (IDE) (21 CFR 812)

d. **The Assurance and IRB Registration Process.** The Stratton VA Medical Center has an approved OHRP Federal Wide Assurance (FWA) of compliance with HHS regulations for the protection of human subjects (FWA #00002073). The IRB is registered with OHRP (IRB #00000950).

TYPES OF HUMAN SUBJECT RESEARCH AND INSTITUTIONAL REVIEW BOARD (IRB) CONSIDERATIONS

All VA research involving human subjects must be reviewed prospectively by an Institutional Review Board (IRB).

Determining the Identification of 'Human Subjects Research'

When a potential or existing researcher wishes to initiate a new protocol, they may meet with the HRPP coordinator to determine if the protocol must be presented to the IRB when there is a question as to whether the proposal is research and more particularly human subjects research.

The following items are asked orally or by email by the HRPP Coordinator and ACOS/R (or designate) prior to determining if a protocol is to be submitted to the IRB for review:
If ANY of the following are true, the research activity involves human subjects:

- The activity involves a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual.
- The activity involves a living individual about whom an investigator (whether professional or student) conducting research obtains identifiable private information .

- The activity involves a living individual who is or becomes a participant in research, either as a recipient of an investigational drug, as an individual on whom or on whose specimen an investigational device is used, or as a control, or for bench-top analysis.

*A “human subject” may either be a healthy human or a patient and is synonymous with “subject,” “participant,” and “volunteer.”

The determination made by the ACOS/R and HRPP Coordinator is communicated via email or official letter signed by the ACOS/R, if requested.

Examples of Human Subject Research. The following examples illustrate common types of human subject research that may be conducted at the Stratton VA Medical Center, and may be done at one VAMC or conducted as multi-center projects (i.e., VA Cooperative Studies Program): clinical research, behavioral and social sciences research, epidemiological research, repository research, tissue banking, databases, quality assurance/quality improvement activities, surveillance activities, pilot studies, and human genetic research.

The IRB Chair or designee will determine if the research proposal meets the definition of human subject research. This is determined when the application for an IRB review is received. Information required will be submitted according to the Initial Review Checklist. The Chair or designee will make the decision if it meets the definition of research and human subject research as defined according to the DHHS, DVA or FDA definitions. If it is determined to be human subject research, then it will be processed and reviewed by the IRB. If not, then the requestor (PI) will be notified in writing by the IRB Chair or designee.

Selected types of research are exempt from Institutional Review Board review because they are considered to pose no risk to subjects. The IRB Chair or designee makes this determination, not the Principal Investigator. However these studies are reviewed and approved by the Stratton VA Medical Center Institutional Review Board.

> Research activities involving “no more than minimal risk” and in which the involvement of human subjects will be in one or more of the identified categories identified as ‘exempt’ may be reviewed using an expedited review procedure by the IRB Chair or designee (voting members of the IRB with at least one-year of experience on the IRB). If the proposal meets the criteria for expedited review, the IRB Chair or designee conducts the review and reports the findings at the next full committee meeting. Studies that are qualified as ‘exempt’ receive review by the IRB Chair.

All research that is not eligible for exempt review or minimal risk (expedited) review must be reviewed by the full Institutional Review Board.

INSTITUTIONAL REVIEW BOARD ADMINISTRATION

Shared Responsibilities for Protecting Human Subjects

The ethical conduct of research is a shared responsibility. It requires cooperation, collaboration, and trust between the institution, investigators and their research staff, the subjects who enroll in research, and the Institutional Review Board (IRB) members and staff. A clear delineation of the responsibilities of each of these parties in the IRB SOP helps assure protections for the subjects who volunteer for research.

a. **The Medical Center Management (38 CFR 16.103).** The Medical Center Director of the facility is the Institutional Official (IO) and is ultimately responsible for overseeing the protection of human subjects within the facility. The Institutional Official must also ensure that open channels of communication are maintained between the IRB, research investigators and staff, and facility management, and that the IRB is provided with sufficient meeting space and staff to support its substantial review and confidential record keeping responsibilities.

b. **The Institutional Review Board (IRB).** The Institutional Review Board is a formally established subcommittee of the Research and Development (R&D) Committee. (M-3, Part 1, Chapter 2.02 and 3.01). The IRB is an appropriately constituted group that the VA has designated to review and monitor research involving human subjects to protect the rights and welfare of the subjects. The IRB also provides oversight and monitoring of such protections.

   The IRB is also the scientific review body for all research activities. The IRB Committee re-evaluates, at least annually, the scientific quality of all research studies involving human subjects to ensure the protection of human subjects. The Director, with assistance of the ACOS/R, assures that IRB members and other reviewers have adequate experience and credentials to properly participate in this process.

   Membership on the IRB is supplemented, as needed, by consultants or permanent members who possess additional expertise that may be required to perform the scientific review. In accordance with the Common Rule, VA and FDA regulations, the IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove research. Members of the IRB receive various regulatory and historical background reference information and complete training on Human Research Protections as outlined in the IRB member training policy. They also have access to electronic versions of recommended reading

materials on the Stratton VA Medical Center research website and in the Research Office.

The Medical Center recognizes the IRB as the reviewing body for ethical issues involving research protocols, and the FDA recognizes the IRB as its reviewing body at the local level, established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the Stratton VA Medical Center. All research involving human subjects conducted completely or partially in this VA facility must be reviewed and approved by the Stratton VA Medical Center Institutional Review Board .

Specifically, the IRB is responsible for:

- review and evaluation of the reports and results of compliance assessment and quality improvement activities;
- implementation of needed improvement and follow-up on actions, as appropriate;
- monitoring changes in VA and other Federal regulations and policies that relate to human research protections.

The ACOS for Research and Development assesses the qualifications and experience of the IRB Chair prior to making a recommendation to the Medical Center Director. The Medical Center Director appoints the members of the IRB based on recommendations by IRB members and R&D members.

c. **The Research and Development Committee (R&D).** The R&D Committee reports to the Medical Center Director, who is the Institutional Official accountable for all research activities conducted at the Stratton VAMC in Albany. The R&D Committee is responsible for assuring the scientific quality and appropriateness of all research involving human subjects, the protection of human subjects, the welfare of animal research subjects, and laboratory safety. This is accomplished through the review of scientific reviews provided by each subcommittee. The R&D Committee assesses the impact of potential research proposals on the Stratton VA Medical Center, and Care Lines, and advises the ACOS/R&D and the Medical Center Director on professional and administrative aspects of proposals. The R&D Committee cannot alter an adverse report or recommendation, e.g., disapproval for ethical or legal reasons, made by the Institutional Review Board. The Medical Center Director receives an approved signed copy of the minutes of the Research and Development Committee.

If, in the course of its review, the R&D Committee requires changes to the protocol that may affect the protection of the human subjects, the R&D

Committee must refer those changes for the protection of human subjects to the IRB for its approval before the final approval of the R&D Committee.

All proposed research involving human subjects must be reviewed and approved by the Medical Center Institutional Review Board and the Research and Development Committee prior to the initiation of the study. VA patients may also be recruited for non-VA studies. Research reviewed by the IRB Chair or designee or the full committee is reported in the IRB minutes to the R&D Committee.

Members of the Research and Development Committee receive various regulatory and historical background information and complete the same training as IRB members. They also have access to electronic versions of recommended reading materials on the Stratton VA Medical Center research website and in the Research Office.

d. **The Principal Investigator** As the individual responsible for the implementation of research, the principal investigator assumes direct responsibility for ensuring the protection of every research subject enrolled in the study. This responsibility starts with protocol design, which must minimize risks to subjects while maximizing research benefits. In addition, the principal investigator must ensure that all members of the research team always comply with the findings, determinations, relevant policies and regulations listed above, and requirements of the IRB. The principal investigator must also ensure the adequacy of both the informed consent document and the informed consent process, regardless of which members of the research team are authorized to actually obtain and document consent.

Principal investigators are responsible for ensuring that (1) all human subject research that they conduct for the VAMC, as employees or agents of the VA, has received initial review and approval by the IRB; (2) once the study is approved, continuing review and approval of the research has been obtained appropriate to the degree of risk and not less than one time per year; and (3) the research is conducted at all times in compliance with all applicable regulatory requirements and the determinations of the IRB. The IRB will not retroactively approve research conducted with human subjects.

No changes in approved research may be initiated without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to subjects; and no research may be continued beyond the IRB-designated approval period (38 CFR 16.103).

Investigators must notify the IRB promptly of (1) any serious adverse events or unanticipated problems involving risks to subjects or others, and

(2) any serious or continuing non-compliance with applicable regulatory requirements or determinations of the IRB (21 CFR 56.108(b) and 38 CFR 16.103).

Federal regulations, organizational policies/procedures, and IRB(s) exist to enhance, but cannot replace the investigator's primary role as the protector of the rights and welfare of research subjects.

Investigator responsibilities are listed in the Investigator Responsibilities SOP and can be found on the research website.

Qualifications of Investigators. The Institutional Review Board will consider research proposals submitted by qualified investigators who are employees of the Stratton VA Medical Center, or who hold a WOC appointment. The investigator's CV is reviewed in relation to the degree of protocol complexity and risk to human subjects. The IRB may require that experienced VA researchers serve as mentors for less experienced research investigators. Proposals that require skills beyond those held by the PI either will be modified to meet the investigator's skills, will have qualified personnel added, or will be disapproved. In general, all physicians and employees with advanced degrees will be considered to be qualified investigators by the IRB if they meet all educational/training requirements, have concurrence from their Care Line Manager, and submit curriculum vitae. The PI must have the appropriate educational training and be credentialed to conduct research involving human subjects by a program that meets all VA requirements.
An investigator from outside the Stratton VA Medical Center who would like to be a PI on a study must have a VA collaborating primary PI on the study, meet the above-described qualifications, and must receive approval from their care line manager or supervisor, as appropriate. Residents and other health professionals in training programs must have a responsible VA investigator as the primary Principal Investigator on a research study.
The investigators have a strict obligation to comply with all IRB determinations and procedures, adhere rigorously to all protocol requirements, inform staff of all adverse events or unanticipated problems, ensure the adequacy of the informed consent process, and take measures necessary to ensure adequate protection for subjects by other members of the research team.

e. **Other Members of the Research Team.** Each member of the research team is responsible for human subject protection. Co-investigators, sub-investigators, study coordinators, nurses, research assistants, and all other research staff have a strict obligation to comply with all IRB determinations and procedures, adhere rigorously to all protocol requirements, inform investigators of all adverse subject reactions or unanticipated problems, ensure the adequacy of the informed consent

process, and take measures necessary to ensure adequate protection for subjects.

Every member of the research team is responsible for notifying the IRB promptly of any serious or continuing non-compliance with applicable regulatory requirements, or determinations of the designated IRB, of which they become aware, whether or not they themselves are involved in the research.

IRB Roles and Authorities

Department of Veterans Affairs (DVA) Institutional Review Board derives authority from both regulatory and institutional sources.

a. **Human Subject Protections under VA Regulations** VA regulations at 38 CFR 16 and 17 require protections for human subjects in accordance with the Federal Policy (Common Rule) for the Protection of Human Subjects. The regulations require that each VA Medical Center (VAMC) conducting human subject research file a written Assurance of protection for human subjects with VA and the Office for Human Research Protections (OHRP), designating an Institutional Review Board as the IRB of record. The Office for Human Research Protections also requires completion of online educational modules located on the OHRP web site as part of the terms and conditions of Assurance for Federal Wide Assurance (FWA) signatory officials. The VA Network Director and Medical Center Director complete module one of the OHRP online training modules.

b. **Institutional Authority of the IRB** The VAMC Director is responsible for all research activities conducted under the auspices of the medical center. The Research and Development (R&D) Committee, which reports to the VAMC Director, oversees the designated IRB to review the facility's human subject research protection program.

   The Institutional Official (IO) is the Medical Center Director. The IO is the VA official responsible for ensuring that the HRPP at the facility has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects research. The IO is legally authorized to represent the institution, is the signatory official for all Assurances, and assumes the obligations of the institution's Assurance. The IO is the point of contact for correspondence addressing human subjects research with OHRP, FDA, and VA Headquarters.

   VA policy does not permit use of central commercial IRBs or other non-VA Federal IRB(s).

c. **Scope of the IRB's Authority** The IRB designated by the VAMC Director and named in the FWA has the authority to approve, require modifications in, or disapprove human subject research (38 CFR 16.109(a)) conducted at the Stratton VA Medical Center. The research may be conducted by VAMC salaried employees or agents, or otherwise under the auspices of the VA (e.g., research using non-public patient data from VA records, using VA resources, published or presented with VA cited as supporting or conducting the research, or recruiting VA patients at VA facilities).

The IRB has the authority to take any action necessary to protect the rights and welfare of human subjects in the VA facility's research program and may suspend or terminate the enrollment and/or the ongoing involvement of human subjects in the research as it determines necessary for the protection of those subjects (38 CFR 16.113).

The IRB has the authority to observe and/or monitor human subject research to whatever extent it considers necessary to protect human subjects, including the review of the informed consent process and procedures used to enroll subjects, and the overall conduct of research.

All research performed at the Stratton VA Medical Center will have the approval of the R&D Committee, irrespective of the status of approval or activity of the research at other sites. When human subject research is a component or the sole purpose of the study, the review and approval process by the IRB will take place according to the policies and procedures of the Stratton VA Medical Center.

d. **Report of IRB Findings and Appeal of IRB Determinations** The IRB must provide the investigator with a written statement of its reasons for disapproving or requiring modifications in proposed research, and must give the investigator an opportunity to respond in person or in writing. The IRB evaluates the investigator's response in reaching its final determination.

Notification of IRB contingent approval will include a list of all IRB stipulations that must be met before final IRB approval can be given. Once the IRB has determined that all contingencies have been met, notification of final approval will be made by the IRB Chair or designee.

e. **Other Relationships within the VAMC.**

(1) The IRB may require that proposed research be reviewed and approved by the Albany VAMC's Radiation Safety Committee, the SRS&B Committee, Medication Use Committee, and/or any other relevant committee of the Stratton VA Medical Center.

(2) All persons conducting research within the Stratton VA Medical Center, and all persons acting as employees or agents of the Stratton VA Medical Center regardless of location, must comply with all requirements of the IRB in the conduct of human research. Such persons must provide the IRB with copies of any reports or correspondence to or from any regulatory or compliance enforcement Federal agency, such as ORO, OHRP, or the Food and Drug Administration (FDA), that exercises oversight over the protection of human subjects in research in which they are involved.

f. **Responsibilities to Regulatory Agencies.** The IRB complies with the requirements of all relevant regulatory and compliance enforcement agencies or offices, including ORO, OHRP, and FDA. Copies of any relevant reports or correspondence to or from such agencies concerning the VAMC's research must be provided by the IRB to the VAMC's Director, who shall determine whether any additional notifications are necessary.

(1) **Allegations of Non-compliance.** Within the VA Medical Center structure, allegations of serious non-compliance will be processed according to policy.

(2) **Scientific Research Misconduct.** The Stratton VA Medical Center bears primary responsibility for the prevention and detection of research misconduct within its own facility and for conducting inquiries and investigations when required. The VA has procedures for handling allegations of scientific misconduct.

g. **Responsibility for Human Subject Protection Education Program.** VA policy requires education about human subject protections for research investigators and their research staff. The institutional policy is created by the IRB Chair or designee, HRPP Coordinator, and the Research Compliance Officer, in collaboration with the ACOS-Research. Training records are maintained by the Research Office.

h. **Accessing Legal Counsel:** Legal Counsel is an important adjunct to the HRPP. Key members of the research community in addition to the Director and COS (including: ACOS R&D, Chair R&D, Chair IRB, and Research Service Administrative Officer) are authorized to access Regional Counsel for advice on research issues.

(1) Issues of state versus federal law, conflict of interest, interpretation of regulations and the legal implications of decisions under consideration may all be issues for referral to Regional Counsel. Determinations regarding surrogate consent, grant agreements,

and legally authorized representatives are within the scope of issues for Regional Counsel.

i. **Auditing and Quality Improvement** – Continuous improvements are made to the HRPP Program that are relevant to its needs. Quality assurance processes evaluate whether the organization follows its policies and procedures and achieves the intended outcomes.

(1) Auditing and Quality Improvement by the Research Compliance Officer (RCO)

(2) Audits (random, select and for-cause) of recurring processes are done by the RCO which may include: review of research records, case histories and source documents for compliance with written procedures; reviews of consent documents; review of audits by other entities within the institution

(3) The RCO reports the results of these audits to the IRB

(4) The IRB may take actions that may require modifications or further evaluations. The IRB may have the RCO re-audit to monitor effectiveness and report back to the IRB.

(5) Quality Improvements by the R&D Committee: Review by the R&D may include: review of facility RCO reports; subcommittees' workload and resources; survey of investigators

i. The R&D may take actions based on the data collected and implement these actions and then determine a plan to measure the effectiveness of the changes.

j. **Quality Improvements by the IRB Committee:** Review by the IRB may include: members' attendance, members' CV's, the number and type of reviews by the Chair/members and COI disclosures

Standard Operating Procedures specific to Department of Defense (DOD) Research

- When conducting multi-site research, a formal agreement between institutions is required to specify the roles and responsibilities of each party.
- When survey research involves Department of Defense personnel including U.S. military personnel:
  - Surveys typically require Department of Defense Survey Review and approval.
  - When appropriate, the research project is reviewed and approved by the IRB prior to Department of Defense approval.
- When performing research with a DOD related protocol, an experimental subject will be defined as: An experimental subject is any research subject who is part of the experimental arm of a

protocol. A subject who is part of the control arm of a protocol is not considered an experimental subject.